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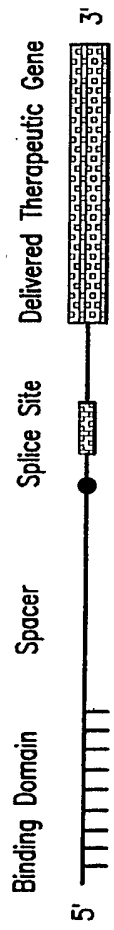


FIG. 1A

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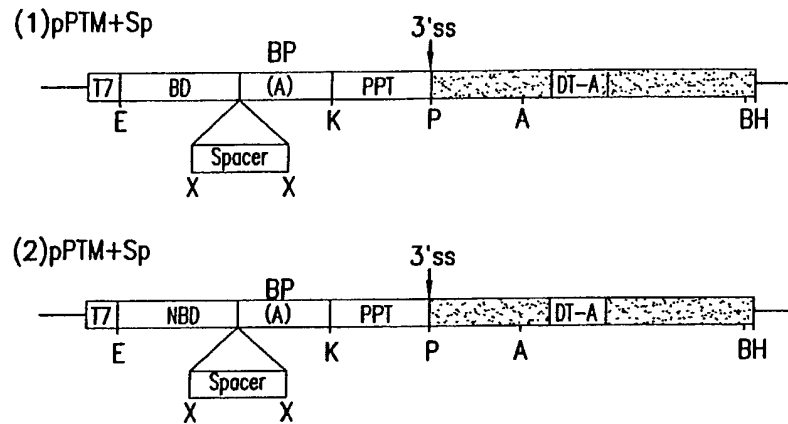


FIG.1B

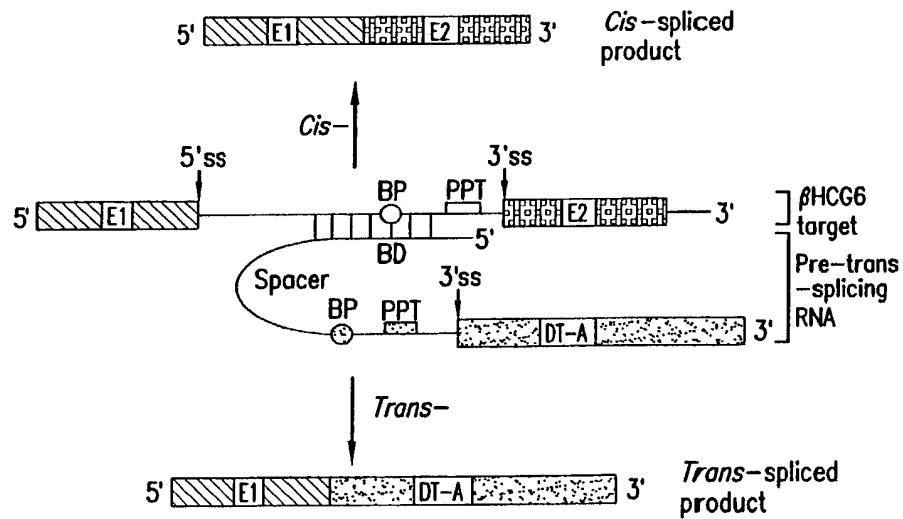
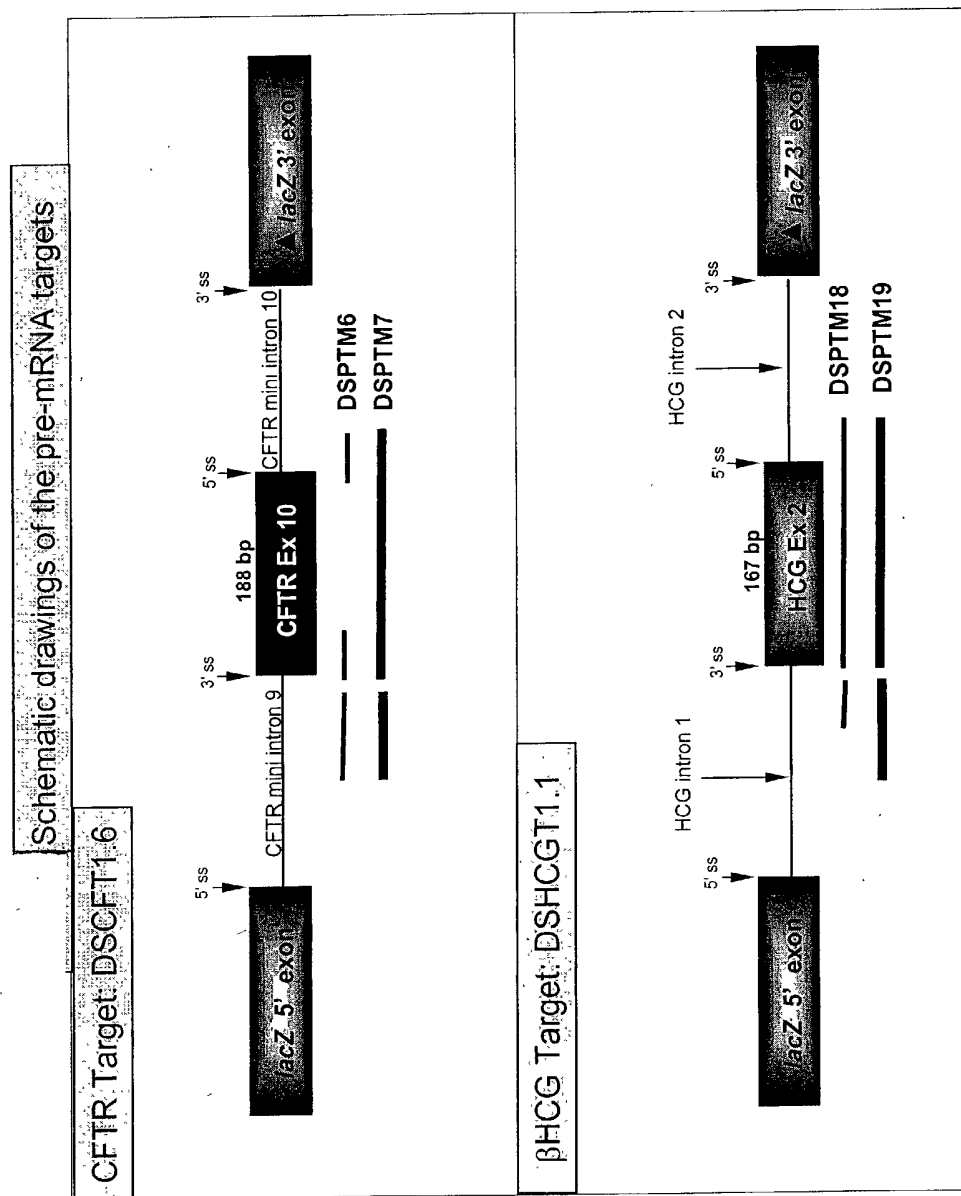


FIG.1C

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Figure 2



$\frac{d}{dt} \left(\int_{\Omega(t)} u^k dx + \sum_{j=0}^{n-1} \alpha_j \right) = - \int_{\partial \Omega(t)} u^k ds$

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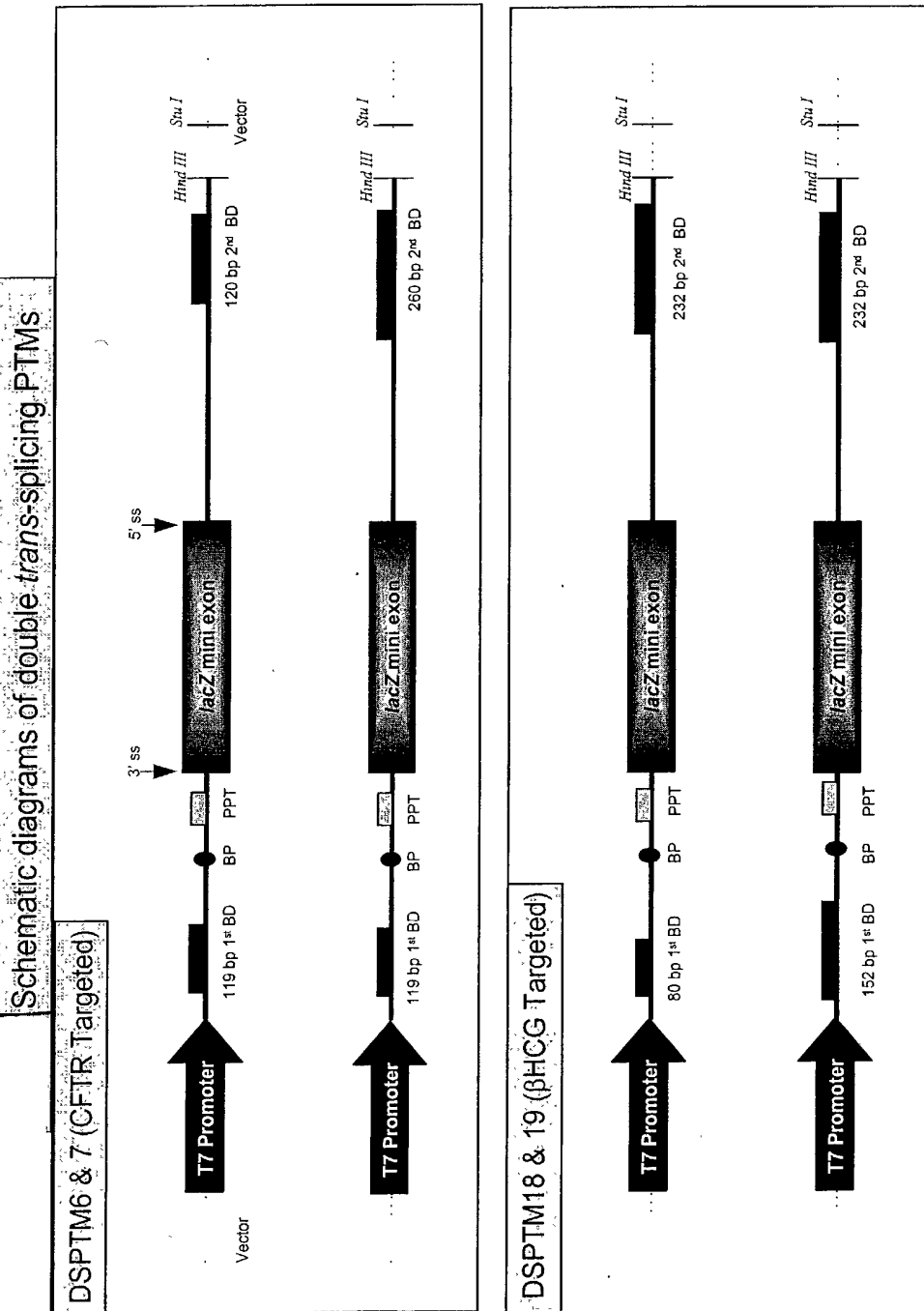
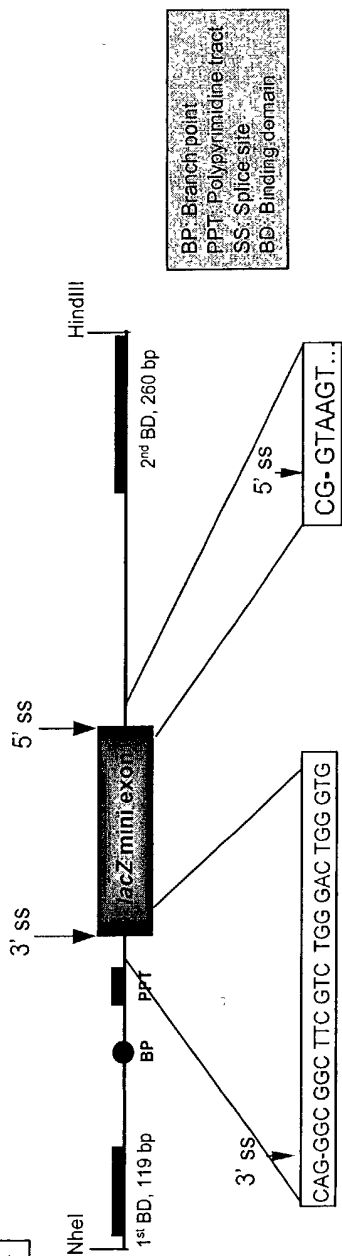


Figure 3

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DSP™-7



1st BD (119 bp) : GATTCACCTGCTCCAAATTATCATCTCAAGCAGAAGTGATATCTTATTTGTAAGATTCATTAACTCATTTGATCAAAATA
TTTAAATACTTCTCGTTTTCATACCTGCTATGCAC

Spacer sequences: AACATTATTATAACGTTGCTCGAA

BP, PPT and acceptor splice site: TACTAAC T GGTACC TCCTCTTTTTTTT GATATC CTCGAG GGC GGC TTC GTC TGG GAC TGG

lacZ mini exon 5' ss
5' donor site and 2nd spacer sequence: TGA ACG GTAAGT GTTATCACCGATATGTCTAACCTGATTGGGGCCTTCGATACGCTAA
GATCCACCGG

2nd BD (260 bp): TCAAAAAGTTTTCACATAATTTCTTACCTCTCTTGAAATTCATGCTTTGATGACGCTTCGTATCTATATTCATCATTTGGAAACACCAATGATTTTTCTTTAATGGTGCCTGGCATAATCCTGGAAGCTGATAACACAATGAAATTTCTTCCAATGTGCTTAAAAAAACCTCTGAATTCCTCAATTTCTCCCATATTCATTTACAACCTGAACTCTGGAATAAAACCCATCATTTATTAACCTCATATCAAAATCACGC

Figure 4

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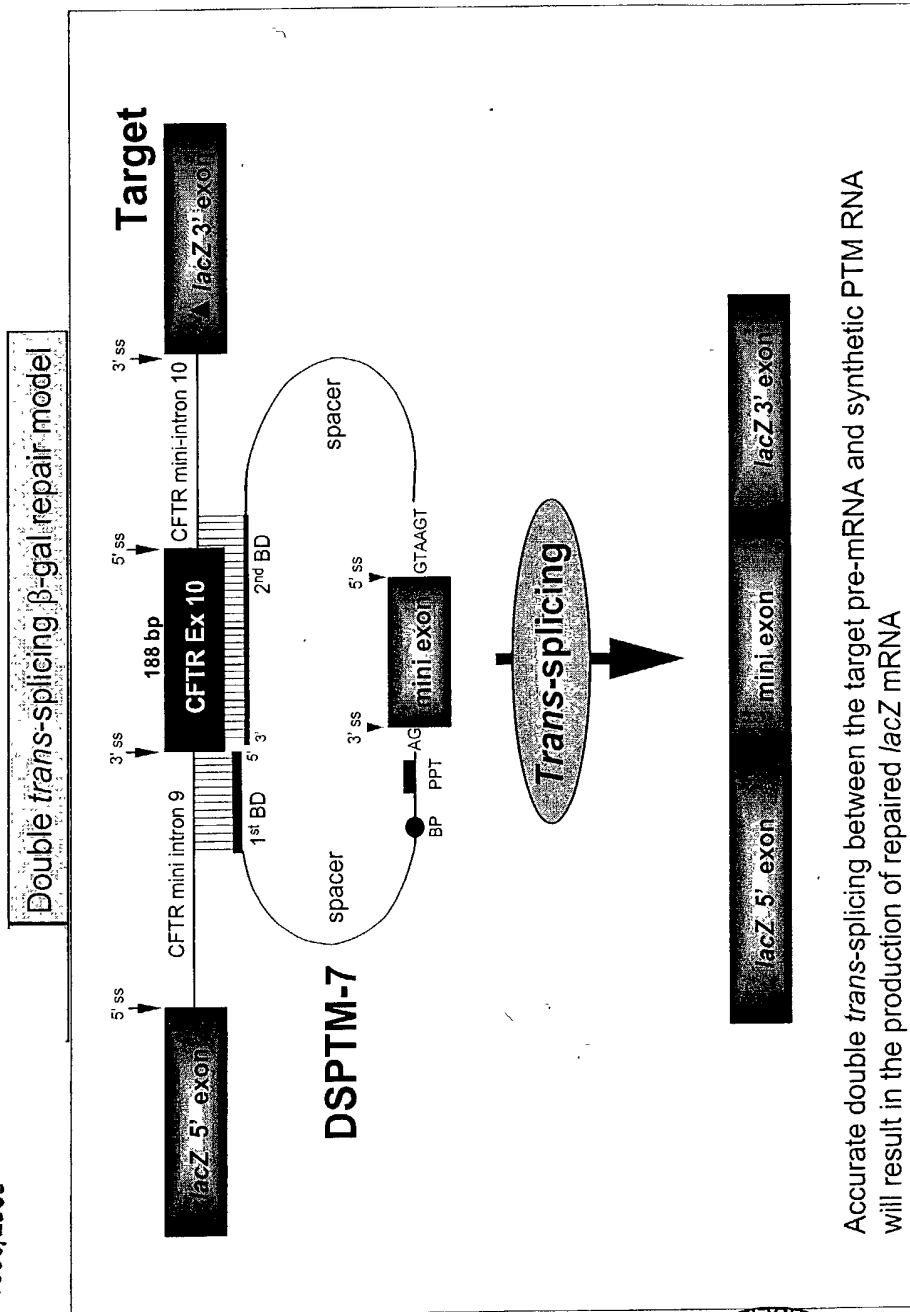
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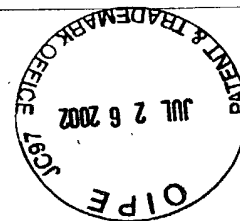
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Figure 5



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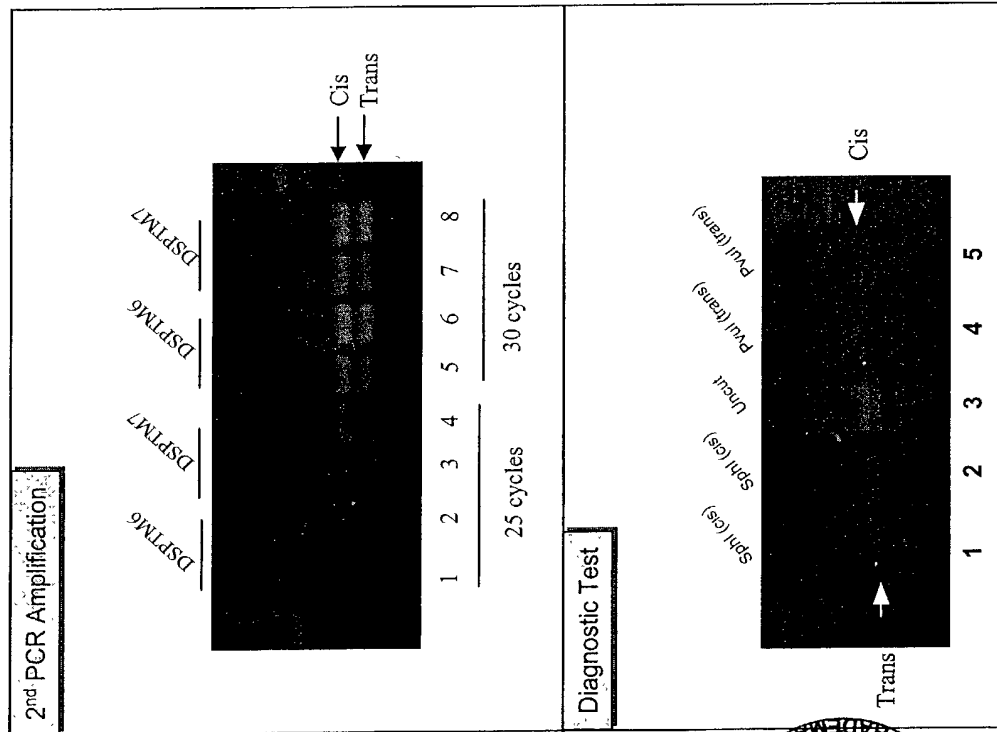
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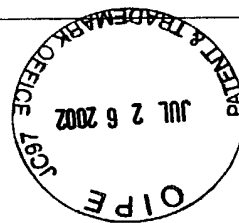
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Proof-of-principle of SMaRT using synthetic double-splicing PTM RNA in 293T cells



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DSPTM6 and 7 (CFTR targeted)

Methods

Transfect 293T cells with DSPTM6 and DSPTM7 *in vitro* transcribed, gel purified RNA (2.5-5.0 μ g)

Isolate total RNA, cDNA synthesis (Lac6R), PCR amplification (20 cycles, KI-1F + Lac6R), digest with *Sph* I + *Dde* I (*cis*-specific) at 37°C/ON

Purify double trans-spliced product using Biotin-Lac21R probe

PCR amplify the captured trans-spliced product (KI-2F+Lac6R). Expected products: *cis*- 260bp; *trans*- 220 bp.

Diagnostic test: Digest PCR product with *Pvu* I (*trans*-specific) and with *Sph* I (*cis*-specific) at 37°C for 2-3 hr

Sequence to confirm the accuracy of double trans-splicing

Figure 6A

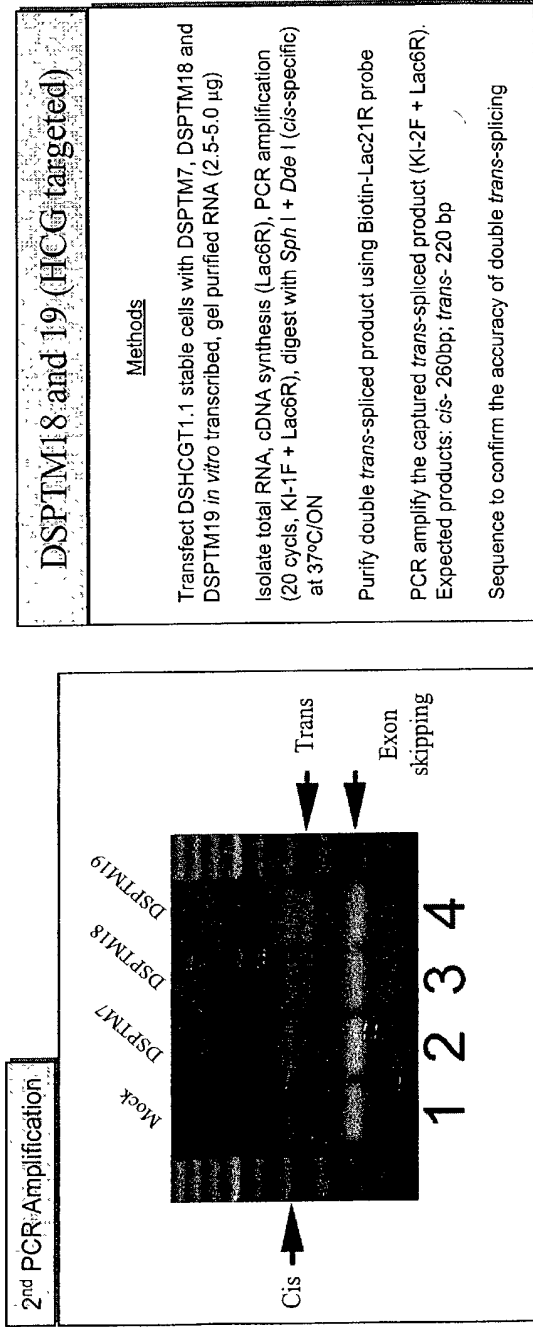
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Proof-of-principle of SMaRT using synthetic double splicing PTM RNA in stable cells



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Figure 6B

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Accuracy of double *trans*-splicing of synthetic PTM RNA in 293T cells

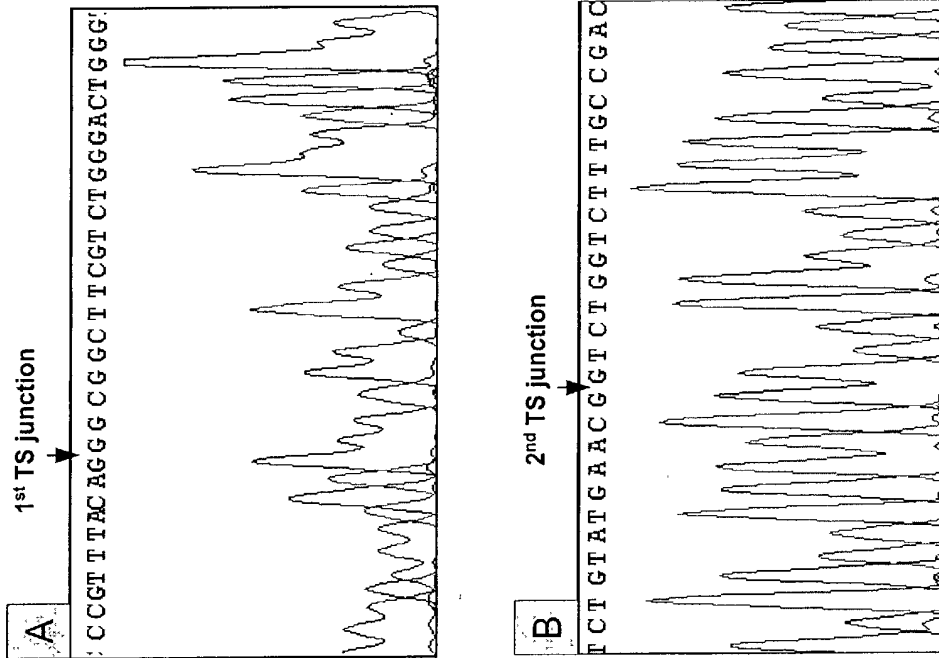


Figure 6C

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Restoration of β -gal function through RNA transfection in 293T cells
(Proof-of-concept for SMaRT RNA Therapeutics!!)
Synthetic RNA, Double trans-splicing

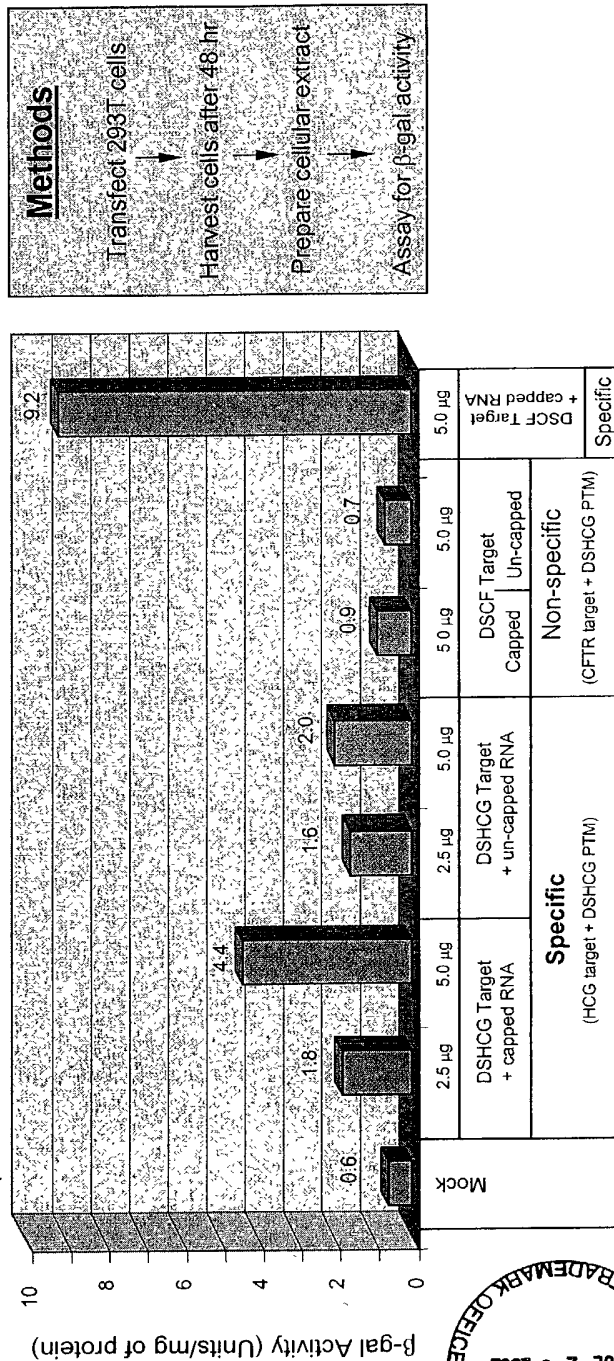


Figure 7

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